REMARKS

I. Status of the Claims

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claims remain under examination in the application, is presented, with an appropriate defined status identifier.

By this Amendment, no new claims have been added, claims 1-48 and 55-56 are cancelled, and claims 49, 50, 51 and 53 are amended. Claims 49-54 are pending. Claims 49, 50, 51 and 53 are amended to provide proper antecedent basis for various claim terms, to more clearly and particularly point out Applicants' invention, and to limit claim 49 to a protein complex comprising SEQ ID Nos: 10 and 15. Because the foregoing amendments do not introduce new matter, entry thereof by the Examiner is respectfully requested.

Applicants respectfully request reconsideration of the present application in view of the forgoing amendments and for the following reasons.

II. A supplemental declaration is being prepared

Regarding the Examiner's objection to the declaration on page 4 of the Office Action, Applicants are currently in the process of preparing a supplemental declaration to be submitted. As the Examiner's objection was not directed towards an issue that appears to require immediate action before continuing prosecution of the present application, this response is being sent with the affirmation that a supplemental declaration will be filed as soon as it is ready to be submitted.

III. The claim objections should be withdrawn in light of the claim amendments

The Examiner objected to claim 49 as being improperly dependent from non-elected claim 46 and for containing recitation of non-elected inventions. Claim 49 has been amended to

be an independent claim and recites only the elected species of HDAC1 (SEQ ID NO.: 10) and SWI/SNF Complex 60 kDa subunit (SEQ ID NO.: 15). The Examiner is therefore respectfully requested to withdraw the objection.

IV. The specification provides written description support for the claims.

The Examiner rejected claims 49-54 under 35 U.S.C. 112, 1st paragraph, as failing to comply with the written description requirement. Specifically, the Examiner argues the following points:

(1) The Examiner asserts that the phrase "protein component(s)" recited in the claims allows the claims to be interpreted broadly as including "any single amino acid residue." See page 5, last paragraph.

(2) The Examiner contends that the specification only provides a "general protocol for isolation of TAP-tagged protein complexes," which is "inadequate" to provide written support for screening a molecule that binds to "HDAC1 and SWI/SNF complex 60 kDa subunit or to any of its protein components." See page 6, last paragraph.

(3) Regarding claim 29, the Examiner alleges that Applicants' "claim does not recite a structure (i.e. SEQ ID NOs: 10 and 15) for claimed methods…and the specification does not provide a disclosure of any particular structure to function/activity relationship in the protein complex or any protein component." See page 7, 2nd paragraph.

(4) The Examiner states that there is a "lack of additional representatives of a method for screening." See page 7, last paragraph.

Applicants respectfully traverse this ground for rejection.

A. Applicants' Claims as Amended do not Recite derivative," "fragment," or "variant, and Therefore they Satisfy the Written Description Requirement

Regarding the Examiner's arguments above, the amended claims specifically require the screening method to be directed to a protein complex comprising HDAC1 and SWI/SNF complex 60 kDa subunit proteins, which are disclosed as comprising SEQ ID NOs.: 10 and 15, respectively. All language directed towards a "derivative," "fragment," or "variant" of the HDAC1 and SWI/SNF complex 60 kDa subunit proteins have been removed. In addition to disclosing their sequences, the HDAC1 and SWI/SNF complex 60 kDa subunit proteins are disclosed in the specification. See for example, Tables 1 and 2 on page 51. The specification therefore has ample written description of the claimed protein complex comprising HDAC1 and SWI/SNF complex 60 kDa subunit proteins.

B. Exemplary Screening Methods are Disclosed in the Application

Specifically regarding the Examiner's argument (2) above, the claims are directed towards a method of ***screening*** for a molecule that can bind to a protein complex comprising HDAC1 and SWI/SNF complex 60 kDa subunit. The claims are not directed towards all methods of producing or making the compound. Because the specific sequences for the HDAC1 and SWI/SNF complex 60 kDa subunit proteins are given, it is unnecessary for a plurality of different protein production methods to be disclosed to provide written description support for the claimed ***screening*** method. Moreover, even if protein production methods were required to provide written description for the present claims, the specification discloses such methods in a manner that would allow one or ordinary skill in the art to recognize that Applicants had possession of the invention at the time of filing. For example, the Examiner is directed to paragraphs [0397] to [0398] and [0401] to [0425], which provide at least three examples of different methods (i.e. TAP method, immunoprecipitation, recombinant expression) to obtain the claimed protein complexes. In one method, the proteins can be obtained by performing PCR using suitable primers to obtained sequences specific for HDAC1 and SWI/SNF complex 60 kDa subunit proteins, and then inserting the sequences into a suitable vector for introduction into a

cell system. See paragraphs [0401] to [0406]. Because these methods are well known to one having skill in the art, it is unnecessary to provide a working example of each and every single known method to produce a protein to provide adequate written description for the claims.

C. A Function Associated with the Proteins Used in the Complex of the Claimed Method is Disclosed

Specifically regarding the Examiner's argument (3) above, the Examiner is directed to paragraphs [0002] to [0009] and Tables 1-2, which indicate that the HDAC1 and SWI/SNF complex 60 kDa subunit proteins are part of the beta-amyloid precursor protein (APP) processing pathway, which is implicated in the onset of neuropathological lesions observed in Alzheimer's disease. The specification is clear in stating that molecules or compounds that can potentially affect the beta-APP pathway, including those that bind to HDAC1 and SWI/SNF complex 60 kDa subunit proteins, would be of use for therapeutic or diagnostic purposes for the neuropathological lesions. The structure/function relationship of HDAC1, SWI/SNF complex 60 kDa subunit, and any molecule that binds to the proteins is therefore established for a specific purpose and provides adequate written description for the claimed screening method.

D. Assays and Screening Techniques Encompassed by the Claims are Described

Specifically regarding the Examiner's argument (4) above, the Examiner is directed to paragraphs [0543] to [0557], which describe different types of assays and screening techniques that apply to the claimed invention. For example, molecules that modulate the protein complex activity can be screened by "panning" techniques or a binding inhibition assay. The disclosed methods are known to one having ordinary skill in the art. Although the Examiner cited a lack of "representative methods" in the specification, working examples or detailed description of numerous screening techniques are unnecessary given the state of the art for these methods.

V. The claims are enabled.

Claims 49-54 were rejected under 35 U.S.C. 112, 1st paragraph, as failing to enable the claimed screening method for anything other than a molecule that binds to a protein complex comprising SEQ ID NOs.: 10 and 15 using a Tandem Affinity Purification. Although the Examiner points out the different criteria set forth by the Wands factors (see page 9, 1st paragraph), the Examiner essentially argues criteria (1) the amount of experimentation necessary, (2) amount of direction or guidance presented, and (8) breadth of claims. Specifically, the Examiner states the following:

(1) The Examiner contends that the claims are broad enough to encompass "any method of screening" and do not place "structural limits" on the protein complex. See page 9, 2nd and last paragraphs. The Examiner also states that since knowledge and guidance of "which amino acids in a peptide's sequence, if any, are conserved" and of "ways in which the peptide's structure relates to its function" is necessary for understanding which sequences in a peptide can be used for the invention, and the specification only discloses two peptides, SEQ ID NOs.: 10 and 15, the claimed method is not enabled. See page 9, last paragraph spanning page 10, 1st paragraph.

(2) The Examiner further alleges that the specification "does not support the broad scope of the claims" since the specification does not establish the following elements: (A) regions of proteins that can be modified without affecting its function, (B) general tolerance of protein complex modification, (C) a "rational and predictable" scheme for modifying the protein complex while obtaining the "desired biological function, and (D) which of the "essentially infinite possible choices is likely to be successful." See page 10, 2nd paragraph.

Applicants respectfully traverse this ground for rejection.

Regarding both of the Examiner's arguments above, they focus on the central theme that the specification does not provide guidance or direction in how to determine when a molecule has bound to a modification or fragment of the protein complex, especially when the structure/function relationship for such modifications and fragments have not been disclosed. However, the amended claims specifically require the screening method to be directed at a protein complex comprising HDAC1 and SWI/SNF complex 60 kDa subunit proteins, which are disclosed as comprising SEQ ID NOs.: 10 and 15, respectively, and all language directed towards a "derivative," "fragment," or "variant" of the proteins have been removed. Moreover, in addition to disclosing their sequences, the HDAC1 and SWI/SNF complex 60 kDa subunit proteins are disclosed in the specification. See for example, Tables 1 and 2 on page 51. Therefore, the specification is fully enabled for the claimed method of screening.

Regarding the Examiner's argument that the claims are only enabled for the screening method of a TAP, the Examiner is directed to paragraphs [0543] to [0557], which describe different types of assays and screening techniques that apply to the claimed invention. For example, molecules that modulate the protein complex activity can be screened by "panning" techniques or a binding inhibition assay. In other examples, modulation of the protein complex by a molecule can be determined based on the activity of the complex protein, intercellular location of the complex protein, transcriptional level of a gene, determining physical parameters of complex formation, and Western Blots etc. See paragraphs [0527], [0530], and [0546]. Further examples include expression of component protein genes (both endogenous and those expressed from cloned DNA containing the genes) that can be detected e.g. by using Southern hybridization, restriction endonuclease mapping, etc. See paragraph [0519]. The disclosed methods are known to one having ordinary skill in the art. Although the Examiner cited a lack of "representative methods" in the specification, nothing more than objective enablement is required, and therefore it is irrelevant whether this teaching is provided through broad terminology or illustrative examples. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). In this case, the specification indicates that the disclosed screening

methods are known to those skilled in the art. Such knowledge necessarily renders the application of the claimed protein complex in screening methodology as objectively enabled.

Even if a more detailed description is required, the specification provides representative examples of specific techniques to perform the claimed screening methods that meet the enablement requirement. For example, the Examiner is directed to paragraph [0545], which discloses suitable binding conditions for the screening method, including specific solutions, detergents, and reaction temperatures. In addition, the specification provides reference to various methods apparent to a person skilled in the art for performing screening methods. See paragraphs [0555] to [0557].

The Examiner is therefore respectfully requested to withdraw the enablement rejection.

It is important to note that although the above protein purification and screening methods have been disclosed as known to one of ordinary skill in the art, these statements are directed solely towards establishing written description and enablement of the claimed invention. It was not previously known to screen molecules that bind to a protein complex comprising HDAC1 and SWI/SNF complex 60 kDa subunit, especially since it was only through the protocols disclosed in the specification that the SWI/SNF complex 60 kDa subunit was determined to be a novel part of the Tip60 complex. See the description of the "Third column" and "Fifth column" of Table 1 on page 25.

VI. The claims are not anticipated.

Claims 49-54 were rejected under 35 U.S.C. 102(b) as being allegedly anticipated by Underhill et al (Biol. Chem., 2000) ("Underhill"). Specifically, the Examiner alleges that Underhill teaches exposing "the complexes HDAC1 and SWI/SNF…to N-CoR complexes and determined their binding." See page 13, 2nd paragraph. Specifically regarding claim 51, the Examiner argues that Underhill teaches the claim by disclosing a deacetylase activity assay. See

page 13, last paragraph. Specifically regarding claim 54, the Examiner contends that Underhill teaches a pharmaceutically acceptable carrier by disclosing purified N-CoR complexes contained in 10% glycerol. See page 14, 1st paragraph. Finally, specifically regarding claims 50, 52, and 53, the Examiner argues that the present claims are "included in this rejection because they are drawn to intended "uses" of claimed methods" and do not require additional active steps from claim 49. See page 14, 2nd paragraph. Applicants respectfully traverse this ground for rejection.

Regarding the Examiner's assertion that Underhill teaches complexes comprising HDAC1 and SWI/SNF proteins, Underhill actually fails to teach the specifically claimed protein complex comprising ***both*** the HDAC1 and SWI/SNF complex 60 kDa subunit proteins in one protein complex.

Underhill teaches that two N-CoR complexes were discovered: N-CoR-1 and N-CoR-2. For N-CoR-1, the ***only*** HDAC protein found in that complex was ***HDAC3***. See the abstract, disclosing that "the only HDAC found in the N-CoR-1 complex was HDAC3" and page 40466, left column, last paragraph spanning right column, 1st paragraph, disclosing that HDAC1 and 2 were not retained by the anti-N-CoR immunoaffinity column, suggesting that "they are not intrinsic components of the N-CoR-1 complex." The N-CoR-1 complex cannot there be considered as teaching the claimed protein complex comprising both HDAC1 and SWI/SNF complex 60 kDa subunit proteins.

For N-CoR-2, Underhill teaches the HDAC1 subunit was discovered in that complex, among the 12-15 proteins that were consistently copurified with N-CoR. See page 40468, left column. However, the other protein subunits discovered in N-CoR-2 do not appear to be affiliated with the SWI/SNF family. See the abstract, disclosing that "N-CoR-2 contained predominately HDAC1 and HDAC2 as well as several other subunits that are found in the Sin3A:HDAC complex," and page 40467, disclosing the identification of "the N-CoR-Sin3-HDAC complex." While Underhill does not disclose what all of the "other" subunits are in the N-CoR-2 complex, there is no suggestion or indication that any of them comprise the SWI/SNF

complex 60 kDa subunit. Without specific teaching that the SWI/SNF complex 60 kDa subunit is necessarily a part of the N-CoR-2 complex, the Examiner has not set forth a prima facie case that Underhill anticipates the claimed protein complex. One of ordinary skill in the art at the time of the invention would not have come to the realization that the N-CoR-2 complex comprises both the claimed HDAC1 ***and*** SWI/SNF complex 60 kDa subunit claimed in the present invention.

Regarding the Examiner's argument that claims 50, 52, and 53 comprise "intended uses" of the screening method, Applicants respectfully disagree. Although claim 50 recites language that suggests an intended use of the method, it is clear that the claim actually limits the claimed ***molecule***, by requiring a molecule that "modulates" the complex. Claims 52 and 53 have similar language to claim 50. For claim 52, the language requires the molecule of claim 49 to be a drug that can treat or prevent a disease or disorder. For claim 53, the language requires the molecule to "modulate the apoptotic activity" of the complex in claim 49. All of claims 50, 52, and 53 therefore require a further, narrow interpretation of the claimed molecule in claim 49.

Considering the statements set forth *supra*, the Examiner is therefore respectfully requested to withdraw the rejection.

VII. Conclusion

In view of the forgoing amendments and remarks, Applicants believe that the present application is now in condition for allowance. Therefore, favorable reconsideration and allowance of the application, as amended, is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741.

An extension of time of two months is concurrently submitted to insure timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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